

## REMARKS

Applicants incorporate by reference their August 3, 2009 and March 12, 2010 remarks. Applicants request reconsideration of those arguments in view of the pending claims.

### 35 U.S.C. § 103

The pending claims are directed to methods that detect a megakaryocyte through optics exclusively. The methods generate scattergrams from detected fluorescent light and detected scattered light. The scattergram comprises a predetermined megakaryocyte region. Based on the detected fluorescent light and the detected scattered light, the methods detect megakaryocytes, if a population exists.

Sakata (Sysmex Journal International 2000) in view of Houwen (US 5,830,701), Walters et al (Laboratory Hematology 2000), and Ota et al (Haematologia 2000) relate to a nucleated red blood cell (NRBC) measurement. See Sakata, pg. 41. When measurements are carried out, blood is treated with an acidic hypotonic solution containing cationic active agent. See Sakata, pg. 41 (first full paragraph). The agents are "not well suited for electric resistance measurements" and cause 'cell damage' and 'form changes' (See Sakata, pg.

Table 1 Hemolytic agent

Main constituents	Advantages	Disadvantages	Remarks
Hypotonic solution	<ul style="list-style-type: none"><li>• Little damage to leukocytes.</li><li>• Able to maintain cell form and features close to <i>in vivo</i>.</li><li>• RBC are able to be selectively lysed by adjusting the pH of the solution to acidic.</li></ul>	<ul style="list-style-type: none"><li>• RBC are lysed; but since erythrocytic membranes remain as ghosts, it is not well suited for electric resistance measurement method.</li></ul>	<ul style="list-style-type: none"><li>• Popularly used for optical measurement method.</li></ul>
Cationic surface active agents	<ul style="list-style-type: none"><li>• Extremely quick hemolysis reactions.</li><li>• Comparatively small RBC ghosts.</li></ul>	<ul style="list-style-type: none"><li>• Damage to cells is comparatively large and cell form is likely to change.</li></ul>	<ul style="list-style-type: none"><li>• Popularly used for electric resistance measurement method.</li></ul>

43: Table 1). While the proposed combination applies a hypotonic solution that "is not well suited for electric resistance measurements" and cause 'cell damage' and 'form changes' (See Sakata, pg. 43: Table 1) the Official Action asserts that the combination detects hematopoietic progenitor cells (HPC) appearance zone through electrical resistance.

Where the detecting comprises passing the assay through an electrically charged aperture and identifying a change in direct current (DC) resistance and radio frequency (RF) resistance is taught as well as cell size information based on a change in DC and cell interior information based on a change in RF (column 7 lines 2-23).

*Official Action at pg. 6*

Not only are the combination of references not 'well suited,' the combination causes *significant cell damage* by its electrical resistance detection that calls into question the reason to combine the elements in the way the claimed invention does. *Ibid.* It also calls into question the ability of the system to detect the claimed cell populations.

The USPTO Examination Guidelines for determining obviousness under KSR explains that it remains legally insufficient to conclude that a claim is obvious just because each feature of a claim may be independently shown in the cited art. The Guidelines recognize that when art teaches away from combining known elements it more likely to be nonobvious.

Note that combining known prior art elements is not sufficient to render the claimed invention obvious if the results would not have been predictable to one of ordinary skill in the art.<sup>49</sup> "When the prior art teaches away from combining certain known elements, discovery of successful means of combining them is more likely to be nonobvious."<sup>49</sup>

Fed. Reg. Vol. 72, No. 195 at 57529

This is more evident in the pending claims if the detection method (e.g., a resistance measurement) cited by the Official Action is relied on to reject claims that detect megakaryocytes through optics alone. As the proposed combination explains, there is no need to gather information optically, when information is gathered through electrical conductivity.

There is no need to consider electrical conductivity if cell information is to be obtained by optical means alone, for instance, scattered light.

*Houwen, col 6, 39 - 41*

In view of the teachings away from the suggested combination, it is also unreasonable to expect success from such a combination, and therefore, unreasonable to suggest it is 'obvious to try'. See Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* at 57529 (explaining the rationale for 'obvious to try' must have a reasonable expectation of success). For this reason, Applicants respectfully request withdrawal of this rejection.

### **Conclusion**

In view of the remarks above, Applicants respectfully submit that the claimed invention is in condition for allowance. Early notification to such effect is earnestly solicited. If for any reason the Examiner feels that the above Response and Request for Reconsideration does not put the claims in condition to be allowed and that a discussion would be helpful to advance prosecution, it is respectfully requested that the Examiner contact the undersigned attorney directly at (312)-321-4786.

Respectfully submitted,

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